| Fiscal Voar                                  | EV 2016   | Task Last Undated:                          | EV 12/04/2015                                    |
|--|---|---|--|
| PI Name                                      | Devraier Alix C Ph D  | Task Last Opuateu.                          | FT 12/04/2015                                    |
| Project Title                                | Effect of Unloading on the Structure and Machanica  | of the Potetor Cuff Tondon to               | Pono Incortion                                   |
| rioject fille.                               | Effect of Offloading on the Structure and Mechanics   | of the Rotator Curr Tendon-u                | -Bone insertion                                  |
| Division Name:                               | Human Research  |   |  |
| Program/Discipline:                          | NSBRI   |   |  |
| Program/Discipline<br>Element/Subdiscipline: | NSBRIMusculoskeletal Alterations Team   |   |  |
| Joint Agency Name:                           |   | TechPort:                                   | No   |
| Human Research Program Elements:             | (1) HHC:Human Health Countermeasures  |   |  |
| Human Research Program Risks:                | <ol> <li>Bone Fracture: Risk of Bone Fracture due to Sp.</li> <li>Osteo: Risk Of Early Onset Osteoporosis Due To</li> </ol> | aceflight-induced Changes to<br>Spaceflight | Bone   |
| Space Biology Element:                       | None  |   |  |
| Space Biology Cross-Element<br>Discipline:   | None  |   |  |
| Space Biology Special Category:              | None  |   |  |
| PI Email:                                    | alix.c.deymier@gmail.com  | Fax:  | FY 212-342-6193                                  |
| PI Organization Type:                        | UNIVERSITY  | Phone:                                      | 212-305-7965                                     |
| Organization Name:                           | Columbia University Medical Center  |   |  |
| PI Address 1:                                | Department of Orthopaedic Surgery   |   |  |
| PI Address 2:                                | William Black Bldg Rm 14-1408   |   |  |
| PI Web Page:                                 |   |   |  |
| City:  | New York  | State:                                      | NY   |
| Zip Code:                                    | 10032-3702  | <b>Congressional District:</b>              | 13   |
| Comments:                                    | NOTE: Also known as Alix Deymier-Black; former  | affiliation Washington Univer               | rsity School of Medicine (Ed., 3/8/17)           |
| Project Type:                                | Ground  | Solicitation / Funding<br>Source:           | 2013 NSBRI-RFA-13-01<br>Postdoctoral Fellowships |
| Start Date:                                  | 11/01/2013  | End Date:                                   | 10/31/2016                                       |
| No. of Post Docs:                            | 1   | No. of PhD Degrees:                         | 0  |
| No. of PhD Candidates:                       | 0   | No. of Master' Degrees:                     | 0  |
| No. of Master's Candidates:                  | 0   | No. of Bachelor's Degrees:                  | 1  |
| No. of Bachelor's Candidates:                | 2   | Monitoring Center:                          | NSBRI  |
| Contact Monitor:                             |   | <b>Contact Phone:</b>                       |  |
| Contact Email:                               |   |   |  |
| Flight Program:                              |   |   |  |
| Flight Assignment:                           | NOTE: End date is now 10/31/2016 per NSBRI (Ed  | ., 10/13/15)                                |  |
| Key Personnel Changes/Previous PI:           |   |   |  |
| COI Name (Institution):                      | Thomopoulos, Stavros (MENTOR/Washington U   | niversity)                                  |  |
| Grant/Contract No.:                          | NCC 9-58-PF03503  |   |  |
| Performance Goal No.:                        |   |   |  |
| Performance Goal Text:                       |   |   |  |

| Rationale for HRP Directed Research:         Research Impact/Earth Benefits:       Research Impact/Earth Benefits:         Research Impact/Earth Benefits:       Research Impact/Earth Benefits:  | Task Description:                    | <ul> <li>POSTDOCTORAL PELLOWSHIP</li> <li>The goal of this project is o investigate the effect of unloading on the tendon-to-bone attachment at a number of hierarchical scales. At the nanometer scale, I proposed to examine changes in the organization of the bone mineral relative to the collagen fibrils with unloading via Transmission electron microscopy-electron energy loss spectroscopy (TEM-EELS). At a scale on the order of micrometers, I was interested in employing Raman and high-energy nano-x-ray diffraction (XRD) to identify modifications made to the mineral content, composition, structure and organization in the interfacial tissue. Micro-mechanical testing would be employed to examine changes in the mechanics at the micron scale. At the millimeter scale. Micro-computed tomography (µCT) and tensile testing were employed to determine the effects of unloading on bone quantity and quality and tissue mechanics.</li> <li>In the past two years, significant discoveries have been made explaining how the structure and mechanics of the tendon-to-bone attachment vary with unloading. Botulinum Toxin A (Btx) injections into the supraspinatus muscle were employed as an Earthbound model of disuse and unloading. At the millimeter scale, I found that 3 weeks of unloading resulted in a -30% loss in bone volume as measured by uCT. Supringly, this loss was accompanied by a significant increases in tendon elastic modulus. This change in modulus is likely due to a changes in the soft tissue composition during unloading or structural changes at lower hierarchical scales. The tendon-to-bone attachment exhibits a gradient remains unaffected by unloading. However, nano-XRD studies indicate that the gradient region exhibits a variety of changes in microl orstain with unloading, leading to a decrease in ownic orotation with moloading, leading to a decrease in ownic orotation with moloading, leading to a decrease in tissue toughness. Raman measurements of the mineralized token, thuolading results in greater misalignment, an</li></ul>   |  |
|---|--------------------------------------|--|--|
| Task Progress:       Rotator cuff tears are extremely prevalent, especially in the elderly population (~50% prevalence in individuals over 80 years). Even in the best of situations these tears are difficult to repair with a failure rate for repaired rotator cuffs as high as 94%. Rotator cuff tears tend to occur at the interface between dissimilar materials are prone to stress concentrations and increased failure risk. In healthy tissue, a number of structural mechanism such as gradients in mineral content, collagen orientation, and matrix composition suggests that there may be changes in the interfacial structure due to unloading as a result of disuse or decreased use of the shoulder.         Weight and the structure due to unloading as a result of disuse or decreased use of the shoulder.       Understanding how changes in the enthesis structure affect the mechanics of the insertion in loaded and unloaded systems will help us to develop enhanced techniques for treatment and repair. Therefore, the research performed in this project will not only help the astonaut population, but will also provide essential information in regards to the mechanics of rotator cuff tissues and how they respond to use and disuse.         This project focuses on examining the mechanical and structural changes induced in the tendon-to-bone attachment the millimeter scale. In the insite mechanics and mone-meter scale, and the micrometer scale, and the millimeter scale, the micro-meter scale. In the ast year 1 have focused specifically on changes to the attachment at the millimeter scale. Name micrometer scales. In all cases, I employed injections of Botulium Toxin A (Btx) in the supraspinatus muscle, which induces local paralysis, as an analogue for unbading and microgravity. Significant hone loss due to unadiation and structure at the millimeter scale. This includes camining the gradient region of the tendon to bone attachment the compo   | Rationale for HRP Directed Research: |  |  |
| Task Progress:This project focuses on examining the mechanical and structural changes induced in the tendon-to-bone attachment<br>during unloading at multiple length scales. This includes examining the tensile mechanics and bone structure at the<br>millimeter scale, the micro-mechanics and mineral organization, composition and structure at the micrometer scale, and<br>the mineral organization relative to the collagen at the nano-meter scale. In the past year I have focused specifically on<br>changes to the attachment at the millimeter and micrometer scales. In all cases, I employed injections of Botulinum<br>Toxin A (Btx) in the supraspinatus muscle, which induces local paralysis, as an analogue for unloading and<br>microgravity. Significant bone loss due to unloading was measured via µCT. Tensile testing of the loaded and unloaded<br>samples indicated that there is a significant increase in the attachment modulus. Further work to explain this increase in<br>stiffness by examining failure modes and failure area is currently underway.<br>At the micrometer scale, I was interested to unmineralized. X-ray fluorescence and Raman spectroscopy results<br>both indicate that there is no change in the width of this graded region with unloading. However, the composition,<br>structure, and organization of the mineral crystals in the graded region is modified. Nano-X-ray diffraction<br>measurements performed across the graded region show that trends in the mineral ized regions of the attachment the<br>crystal size, compressive residual strain, and crystal alignment increase. However, the unloaded samples exhibit greater<br>misalignment and decreased crystal size. Rotational models showed that these changes induced by unloading resulted in<br>a decreased work of rotation upon loading suggesting a decrease in toughness.At the nanometer scale, Transmission Electron Microscopy–Electron Energy Loss Spectroscopy (TEM-EELS) has been<br>used to examine the location of miner | Research Impact/Earth I              | Rotator cuff tears are extremely prevalent, especially in the elderly population (~50% prevalence in individuals over 80 years). Even in the best of situations these tears are difficult to repair with a failure rate for repaired rotator cuffs as high as 94%. Rotator cuff tears tend to occur at the interface between tendon and bone. Such interfaces between dissimilar materials are prone to stress concentrations and increased failure risk. In healthy tissue, a number of structural mechanisms such as gradients in mineral content, collagen orientation, and matrix composition serve to dissipate these stress concentrations. The increased occurrence of rotator cuff injuries in the elderly population suggests that there may be changes in the interfacial structure due to unloading as a result of disuse or decreased use of the shoulder. Understanding how changes in the enthesis structure affect the mechanics of the insertion in loaded and unloaded systems will help us to develop enhanced techniques for treatment and repair. Therefore, the research performed in this project will not only help the astronaut population, but will also provide essential information in regards to the mechanics of rotator cuff tissues and how they respond to use and disuse.   |  |
|   | Task Progress:                       | This project focuses on examining the mechanical and structural changes induced in the tendon-to-bone attachment<br>during unloading at multiple length scales. This includes examining the tensile mechanics and bone structure at the<br>millimeter scale, the micro-mechanics and mineral organization, composition and structure at the micrometer scale, and<br>the mineral organization relative to the collagen at the nano-meter scale. In the past year I have focused specifically on<br>changes to the attachment at the millimeter and micrometer scales. In all cases, I employed injections of Botulinum<br>Toxin A (Btx) in the supraspinatus muscle, which induces local paralysis, as an analogue for unloading and<br>microgravity. Significant bone loss due to unloading was measured via µCT. Tensile testing of the loaded and unloaded<br>samples indicated that there is a significant increase in the attachment modulus. Further work to explain this increase in<br>stiffness by examining failure modes and failure area is currently underway.<br>At the micrometer scale, I was interested in examining the gradient region of the tendon to bone attachment where the<br>composition transitions from fully mineralized to unmineralized. X-ray fluorescence and Raman spectroscopy results<br>both indicate that there is no change in the width of this graded region with unloading. However, the composition,<br>structure, and organization of the mineral crystals in the graded region is modified. Nano-X-ray diffraction<br>measurements performed across the graded region show that trends in the mineralized regions of the attachment the<br>crystal size, compressive residual strain, and crystal alignment increase. However, the unloaded samples exhibit greater<br>misalignment and decreased crystal size. Rotational models showed that these changes induced by unloading resulted in<br>a decreased work of rotation upon loading suggesting a decrease in toughness.<br>At the nanometer scale, Transmission Electron Microscopy–Electron Energy Loss Spectroscopy (TEM-EELS) has been<br>used to examine the location of min |  |

| <b>Bibliography Type:</b>                 | Description: (Last Updated: 10/19/2020)   |
|---|---|
| Abstracts for Journals and<br>Proceedings | Deymier-Black AC, Schwartz AG, Cai Z, Genin GM, Thomopoulos S. "Role of Mineral Organization on the Mechanics of the Tendon-To-Bone Interface Examined via High Energy X-Ray Diffraction." 2015 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 13-15, 2015. 2015 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 13-15, 2015. , Jan-2015       |
| Abstracts for Journals and<br>Proceedings | Deymier-Black AC, Schwartz AG, Cai Z, Genin GM, Thomopoulos S. "Effect of Unloading on the Organization of<br>Mineral Crystals at the Tendon-to-Bone Attachment." Musculoskeletal Research Center Winter Symposium, St Louis,<br>MO, Feb 16, 2015.<br>Musculoskeletal Research Center Winter Symposium, St Louis, MO, Feb 16, 2015. , Feb-2015  |
| Articles in Peer-reviewed Journals        | Deymier-Black AC, Pasteris JD, Genin GM, Thomopoulos S. "Allometry of the tendon enthesis: Mechanisms of load transfer between tendon and bone." Journal of Biomechanical Engineering. 2015 Nov;137(11):111005.<br>http://dx.doi.org/10.1115/1.4031571; PubMed PMID: 26355607, Nov-2015   |
| Awards                                    | Deymier-Black A. "Musculoskeletal Research Center Winter Symposium Poster Award, February 2015." Feb-2015   |
| Awards                                    | Deymier-Black A. "NSBRI Dr. David Watson Poster Contest Award, January 2015." Jan-2015  |
| Papers from Meeting Proceedings           | Deymier-Black AC, An Y, Schwartz AG, Genin GM, Thomopoulos S, Barber AH. "Micrometer Scale Mechanical<br>Properties of the Tendon-to-Bone Attachment." SB3C. Summer Biomechanics, Bioengineering and Biotransport<br>Conference, Snowbird, Utah, June 17-20, 2015.<br>Proceedings of the 2015 Summer Biomechanics, Bioengineering and Biotransport Conference. Paper number<br>SB3C2015-594. , Jun-2015 |